IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	L.L. Kunz et al.	Examiner:	Unknown
Serial No.:	Unknown	Group Art Unit:	Unknown
Filed:	Herewith	Docket:	295.003US5
Title:	THERAPEUTIC INHIBITOR OF VASCULAR SMOOTH MUSCLE CELLS		

PRELIMINARY AMENDMENT

BOX PATENT APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the above-identified continuation application as follows:

In the Specification

Before the heading "Field of the Invention" at page 1, please insert paragraph 1 in the appendix entitled "Clean Version of Page 1, Paragraph 1". Specific amendments to page 1, paragraph 1 are detailed in the following marked-up paragraph:

Cross-Reference to Related Applications

This application is a continuation of U.S. application Serial No. 09/470,662, filed on December 22, 1999, which is a continuation of U.S. application Serial No. 09/113,733, filed July 10, 1998, now U.S. Patent No. 6,074,659, which is a continuation of U.S. application Serial No. 08/450,793, filed on May 25, 1995, now U.S. Patent No. 5,811,447, which in turn is a continuation of U.S. application Serial No. 08/062,451, filed on May 13, 1993, now abandoned, which in turn is a continuation-in-part of U.S. application Serial No. 08/011,669, filed on January 28, 1993, now abandoned, which in turn is a continuation-in-part of PCT Application No. PCT/US92/08220, filed on September 25, 1992, now completed, which applications are incorporated herein by reference.

In the Claims

Please cancel claims 1-20 without prejudice.

Please add the following new claims:

21. (New) A therapeutic method, comprising treating procedural vascular trauma associated with placement of a device in a vessel by administering to a mammal an amount of a cytostatic agent that does not exhibit substantial cytotoxicity, which agent and amount are selected to allow for vascular repair and extracellular matrix production in the traumatized vessel.

22. (New) A method to inhibit or treat procedural vascular trauma associated with placement of a device in a vessel in a mammal, comprising:
a) providing a cytostatic agent in an selected amount, wherein the selected amount allows for repair and extracellular matrix production in mammalian vascular smooth muscle cells, and wherein the cytostatic agent does not exhibit substantial cytotoxicity; and
b) administering the cytostatic agent to a mammal subjected to vascular trauma in an amount which allows for vascular repair and extracellular matrix production in the traumatized vessel and inhibits or treats procedural vascular trauma.

23. (New) A therapeutic method, comprising treating procedural vascular trauma associated with placement of a device in a vessel by administering to a mammal a cytostatic agent that does not exhibit substantial cytotoxicity in an amount which has a minimal effect on protein synthesis and allows for vascular repair and extracellular matrix production in the traumatized vessel

24. (New) The method of claim 21, 22 or 23 wherein the vessel is subjected to angioplasty, placement of a stent or grafting.

25. (New) The method of claim 21, 22 or 23 wherein the agent inhibits microtubules.

26. (New) The method of claim 21, 22 or 23 wherein the agent inhibits microfilaments.

27. (New) The method of claim 21, 22 or 23 wherein the agent inhibits actin polymerization.

28. (New) The method of claim 21, 22 or 23 wherein the agent is a cytochalasin or an analog thereof.

29. (New) The method of claim 21, 22 or 23 wherein a cytoskeletal inhibitor is administered.

30. (New) The method of claim 21, 22 or 23 wherein the administration is local.

31. (New) The method of claim 21, 22 or 23 wherein the administration is systemic.

32. (New) The method of claim 21, 22 or 23 wherein the administration is before, during or after the trauma.

33. (New) The method of claim 21, 22 or 23 wherein the administration is during the trauma.

34. (New) The method of claim 21, 22 or 23 wherein the administration is accomplished by the device.

35. (New) The method of claim 21, 22 or 23 wherein the administration is accomplished by a catheter.

36. (New) The method of claim 21, 22 or 23 wherein the amount is effective to inhibit migration of vascular smooth muscle cells.

37. (New) The method of claim 21, 22 or 23 wherein the agent is administered in a sustained release dosage form.

38. (New) The method of claim 21, 22 or 23 wherein the agent is administered in a polymeric carrier.

39. (New) The method of claim 37 wherein the sustained release dosage form is biodegradable.

40. (New) The method of claim 21, 22 or 23 wherein the agent is administered in a sustained release dosage form and delivered by the device.

41. (New) The method of claim 37 wherein the sustained release form comprises a binding peptide or protein which specifically binds to smooth muscle cells, stromal cells or extracellular matrix surrounding smooth muscle cells.

42. (New) The method of claim 37 wherein the sustained release dosage form comprises microparticles or nanoparticles.

43. (New) The method of claim 37 wherein the sustained release dosage form comprises a polymer derived from the condensation of alpha-hydroxycarboxylic acids and related lactones.

44. (New) The method of claim 43 wherein the polymer is selected from the group consisting of a polylactide, a polyglycolide, and a copolymer of lactide and glycolide subunits.

45. (New) The method of claim 44 wherein the polymer is poly(lactide co-glycolide).

46. (New) The method of claim 21, 22 or 23 wherein the agent releases nitric oxide.

47. (New) The method of claim 21, 22 or 23 wherein the agent inhibits the proliferation of smooth muscle cells.

48. (New) A method to screen for an agent to inhibit or treat procedural vascular trauma, comprising:
a) selecting a cytostatic agent that does not exhibit substantial cytotoxicity on mammalian vascular smooth muscle cells; and
b) identifying an amount of the cytostatic agent which allows for extracellular matrix production in mammalian vascular smooth muscle cells.

49. (New) The method of claim 21, 22 or 48 wherein the amount of the agent has a minimal effect on protein synthesis.

Remarks

Claims 1-20 having been canceled, and claims 21-49 having been added, the claims now pending are claims 21-49.

Claims 21-49 are supported, for example, by the specification at originally-filed claims 12 and 14-15, and by the specification at page 5, lines 4-21, page 6, lines 14-19, page 7, lines 15-18, page 8, lines 15-20, page 16, lines 28-31, page 23, lines 11-27, page 24, lines 7-19, page 32, lines 17-20, page 48, line 9-14, and page 48, line 36 through page 49, line 3 and page 54, lines 17-23, page 51, lines 3-27, page 51, line 19 and page 54, lines 17-27, page 53, lines 29-31, page 62, line 27 through page 65, line 25, and page 76, lines 8-9, page 4, lines 22-26, page 5, lines 17-18, page 7, lines 1-7 and 10-15, page 8, line 26-page 9, line 6, page 20, line 25-page 23, line 4, page 29, lines 21-29, page 30, lines 6-10, and page 56, line 3-page 57, line 23.

When the Examiner takes up the above-identified continuation application for the first Office Action, consideration of these amendments and remarks is respectfully requested.

Respectfully submitted,

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By their Representatives,

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"Express Mail" mailing label number: EL67164114US
Date of Deposit: July 20, 2001
This paper or fee is being deposited on the date indicated above with the United States Postal Service pursuant to 37 CFR 1.10, and is addressed to The Commissioner for Patents, Box Patent Application, Washington, D.C. 20231.

CLEAN VERSION OF AMENDED SPECIFICATION PARAGRAPHS

THERAPEUTIC INHIBITOR OF VASCULAR SMOOTH MUSCLE CELLS
Applicant: Lawrence L. Kunz
Serial No.: Unknown

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